289. (New) The method of claim 284 or 285, wherein each of said different nucleotide sequences consists of 15 to 200 nucleotides.

290. (New) The method of claim 289, wherein each of said different nucleotide sequences consists of 20 to 100 nucleotides.

291. (New) The method of claim 290, wherein each of said different nucleotide sequences consists of 40 to 80 nucleotides.

292. (New) The method of claim 291, wherein each of said different nucleotide sequences consists of 60 nucleotides.

REMARKS

Claims 1-36, 45-46, 86-90, 157-183 and 212-279 were pending in the application. Claims 2-3, 35, 182, 214-262 and 268-279 have been canceled without prejudice, claims 1, 4-6, 11-12, 30, 36, 89-90, 158-159, 177, 183, and 263-264 have been amended, and new claims 280-292 have been added to more clearly claim the present invention. Upon entry of the above-made amendment, claims 1, 4-29, 31-34, 36, 45-46, 86-90, 157-176, 178-181, 183, 212-213, 263-267 and 280-292 will be pending. A marked version of the amended claims showing changes made is attached hereto as Exhibit A. A clean version of the pending claims, as amended, is attached hereto as Exhibit B.

Claim 1 has been amended to recite that in the method at least one gene in said plurality of different genes comprises an exon possibly having a plurality of different variants, each of said plurality of different variants being a form of said exon generated using a different splice junction of said exon, and wherein the measured expression levels of said different individual exons or different individual multiexons in said gene are sufficient for determining which of said plurality of different variants of said exon is, and which is not, expressed in said cell sample, and determining which of said plurality of different variants of said exon is expressed. Support for the amendment is found in the specification at page 13, lines 13-27 and page 38, lines 10-25. Claim 1 has also been amended to clarify that the claimed method involves measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality of different genes in the genome of an organism. The support for the amendment is found in the specification at page 5, lines 15-19. Claims 4-6, 11-12, 89-90 and 158-159 have been amended accordingly.

Claims 36 and 183 have been amended to make the claim language clearer by deleting the recitation "as continuous variables and represented." Support for the amendment is found in the specification at page 36, lines 5-7. Claims 36, 183, 263 and 264 have also been amended to depend on the appropriate base claims.

Claims 30 and 177 have been amended such that the claims have proper antecedent basis.

New claims 280-292 have been added. Support for the new claims is found in the specification at page 5, line 14 through page 6, line 2; page 8, lines 4-35; page 25, lines 4-27; page 38, lines 10-25.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH SHOULD BE WITHDRAWN

Claims 35-36, 182-183 and 263 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 35-36 and 182-183 are rejected under 35 U.S.C. § 112, second paragraph, because of the phrase "wherein said expression levels are measured as continuous variables." Applicants have canceled claims 35 and 182, and deleted the phrase from claims 36 and 183. The rejection is therefore obviated and should be withdrawn.

Claim 263 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being unclear as to what the phrase "the longest variant of an exon" means. Applicants respectfully direct the attention of the Examiner to the specification at page 13, lines 20-27, for a definition of a variant of an exon and disclosures regarding the length of such a variant. Applicants have also amended the base claims to recite that a variant of an exon is a form of said exon generated using a different splice junction of said exon. It is therefore clear that an exon may have several different splice forms, i.e., variants, when there are several possible 5' and/or 3' splice junctions in the exon, and the longest variant of an exon simply refers to the variant of the exon which spans the nucleotide sequence between the 3' and 5' end splice junctions which are located the farthest apart from each other. The rejection should therefore be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

Claims 1, 4-6 and 45 are rejected under 35 U.S.C. § 102(e) as being anticipated by DeRisi et al., 1996, Nature Genetics 14:457-460 ("DeRisi"). Claims 7-9 are rejected under 35 U.S.C. § 102(b) as being anticipated by DeRisi as applied to claims 1, 4-6 and 45, in light of Roninson et al., U.S. Patent No. 5,811,234 ("Roninson"). Claims 1, 2, 10-12, 22-26, 28-33, 45, 86, 87, 89, 90, 157-159, 169-173, 175-180, 214, 216, 219-221, 223, 225, 238, 240, 243-245, 247, 249, 265, 268 and 274 are rejected under 35 U.S.C. § 102(e) as being anticipated by Friend et al., U.S. Patent No. 6,165,709 ("Friend"). Claims 13, 160, 218 and 242 are rejected under 35 U.S.C. § 102(e) as being anticipated by Friend as applied to claims 1, 2, 10-12, 22-26, 28-33, 45, 86, 87, 89, 90, 157-159, 169-173, 175-180, 214, 216, 219-221, 223, 225, 238, 240, 243-245, 247, 249, 265, 268 and 274, in light of Roninson. Applicants respectfully disagree with the Examiner for the reasons presented below.

A claim is anticipated under 35 U.S.C. § 102 only if each and every element and limitation as set forth in the claim is found, either expressly described or inherently present, in a single prior art reference. *Glaxo, Inc. v. Novopharm Ltd.,* 52. F.3d 1043, 1047 (Fed. Cir. 1995). There must be *no differences* between the claimed invention and the reference disclosure as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991). Anticipation requires that all aspects of the claimed invention were already described in a *single* reference. *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991).

At the outset, Applicants respectfully submit that claims 2-3, 35, 182, 214-262 and 268-279 have been canceled. The rejection of these claims is therefore obviated.

Claims 1, 4-6 and 45 are rejected under 35 U.S.C. § 102(e) as being anticipated by DeRisi. DeRisi teaches determining the relative expression levels of 870 different genes in two cell samples, a tumorigenic cell line and a non-tumorigenic cell line, by measuring the hybridization levels of mRNAs corresponding to each genes using a DNA microarray containing 870 different cDNAs. Thus, in DeRisi, the expression level of an entire mRNA transcribed from a gene is measured by a cDNA clone on its microarray. Applicants respectfully point out that, even though an mRNA transcribed from a gene may comprise more than one exon or may comprise a multiexon, measuring the expression level of the mRNA is not measuring a plurality of different individual exons or different individual multiexons in the gene. For example, from the measured expression level of an mRNA, the

differences in the expression levels of different individual exons in the mRNA cannot be determined. Therefore, DeRisi does not teach measuring *a plurality of different individual exons or different individual multiexons* in each of a plurality of its genes. DeRisi also does not teach distinguishing among different variants of an exon so as to determine which variant(s) are expressed. DeRisi does not teach a method for analyzing exon expression in a cell sample, comprising measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality, wherein at least one gene in said plurality of different genes comprises an exon possibly having a plurality of different variants, each of said plurality of different variants being a form of said exon generated using a different splice junction of said exon, and wherein the measured expression levels of said different individual exons or different individual multiexons in said gene are sufficient for determining which of said plurality of different variants of said exon is, and which is not, expressed in said cell sample, and determining which of said plurality of different variants of said exon is, and which is not, expressed. Therefore, Applicants respectfully submits that DeRisi does not anticipate claims 1, 4-6 and 45, and that the rejection under 37 C.F.R. § 102(e) based on DeRisi should be withdrawn.

Claims 7-9 are rejected under 35 U.S.C. § 102(b) as being anticipated by DeRisi as applied to claims 1, 4-6 and 45, in light of Roninson. DeRisi has been discussed above. Roninson teaches methods for isolating and identifying genetic elements that are capable of inhibiting gene function. Roninson teaches that somatic tissues of higher eukaryotes express mRNAs for about 10,000 genes. The Examiner contends that Roninson's teaching that somatic tissues of higher eukaryotes express mRNAs for about 10,000 genes can be used to supplement DeRisi to anticipate claims 7-9 of the present invention. At the outset, Applicants respectfully point out that such a rejection based on a combination of DeRisi and Roninson is improper. It is well established that anticipation requires that all limitations be described in a *single* reference. Additional references may not be used to supply additional limitations which are not taught in the primary reference. For example, according to *Scripps Clinic & Research Fdn. v. Genentech, Inc.* 927 F. 2d. 1565, 1576 (Fed. Cir. 1991):

> It is sometimes appropriate to consider extrinsic evidence to explain the disclosure of a reference. Such factual elaboration is necessarily of limited scope and probative value, for *a finding of anticipation requires that all aspects of the claimed invention were already described in a single reference: a finding that is not supportable if it is necessary to prove facts beyond those*

> *disclosed in the reference in order to meet the claim limitations*. The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill in the field of the invention, not to fill gaps in the reference.

(emphasis added). Applicants respectfully submit that DeRisi, as agreed by the Examiner, does not teach measuring, e.g., 1000 or 10,000 different genes. In fact, DeRisi clearly teaches that expression levels of 870 genes are measured using its microarray. Thus, supplementing DeRisi with the teachings of Roninson amounts to "to prove facts beyond those disclosed in the reference in order to meet the claim limitations." Such a use of Roninson to supplement DeRisi as the ground for an anticipation rejection is improper. Furthermore, Applicants respectfully submit that, irrespective of the appropriateness of the combination, the claims are not anticipated by DeRisi and Roninson in that neither DeRisi nor Roninson teaches analyzing the exon expression of a cell sample as claimed. Neither DeRisi nor Roninson teaches measuring a plurality of different individual exons or different individual multiexons in each of a plurality of genes. Neither DeRisi nor Roninson teaches distinguishing among different variants of an exon. Neither DeRisi nor Roninson teaches a method for analyzing exon expression in a cell sample, comprising measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality, wherein at least one gene in said plurality of different genes comprises an exon possibly having a plurality of different variants, each of said plurality of different variants being a form of said exon generated using a different splice junction of said exon, and wherein the measured expression levels of said different individual exons or different individual multiexons in said gene are sufficient for determining which of said plurality of different variants of said exon is, and which is not, expressed in said cell sample, and determining which of said plurality of different variants of said exon is, and which is not, expressed. Therefore, Applicants respectfully submits that the rejection of claims 7-9 under 37 C.F.R. § 102(b) based on DeRisi and Roninson is erroneous, and should be withdrawn.

Claims 1, 2, 10-12, 22-26, 28-33, 45, 86, 87, 89, 90, 157-159, 169-173, 175-180, 214, 216, 219-221, 223, 225, 238, 240, 243-245, 247, 249, 265, 268 and 274 are rejected under 35 U.S.C. § 102(e) as being anticipated by Friend. Friend teaches methods for identifying targets of a drug in a cell. In Friend, the effects of a drug on a cell can be determined by measuring gene expression, protein abundances, and protein activities. Friend teaches that the expression levels of a plurality of genes in a cell sample can be measured using a DNA

array containing one or more binding sites for the mRNA transcribed from each gene. Thus, Friend teaches measuring the expression level of each of a plurality of genes rather than the expression levels of individual exons or multiexons in each of a plurality of genes. Friend does not teach analyzing the exon expression of a cell sample as claimed. Friend does not teach measuring *a plurality of different individual exons or different individual multiexons* in a gene. Friend does not teach distinguishing among different variants of an exon. Friend does not teach a method for analyzing exon expression in a cell sample, comprising measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality, wherein at least one gene in said plurality of different genes comprises an exon possibly having a plurality of different variants, each of said plurality of different variants being a form of said exon generated using a different splice junction of said exon, and wherein the measured expression levels of said different individual exons or different individual multiexons in said gene are sufficient for determining which of said plurality of different variants of said exon is, and which is not, expressed in said cell sample, and determining which of said plurality of different variants of said exon is, and which is not, expressed. Therefore, Applicants respectfully submits that Friend does not anticipate the claims, and that the rejection under 37 C.F.R. § 102(e) based on Friend should be withdrawn.

Claims 13, 160, 218 and 242 are rejected under 35 U.S.C. § 102(e) as being anticipated by Friend as applied to claims 1, 2, 10-12, 22-26, 28-33, 45, 86, 87, 89, 90, 157-159, 169-173, 175-180, 214, 216, 219-221, 223, 225, 238, 240, 243-245, 247, 249, 265, 268 and 274, in light of Roninson. Applicants have pointed out above that a rejection under 35 U.S.C. § 102 based on a combination of DeRisi and Roninson is improper. For the same reasons, a rejection based on a combination of Friend and Roninson is also improper. Applicants also respectfully submit, irrespective of the appropriateness of the combination, the claims are not anticipated by Friend and Roninson in that neither Friend nor Roninson teaches analyzing the exon expression of a cell sample as claimed. Neither Friend nor Roninson teaches measuring a plurality of different individual exons or different individual multiexons in each of a plurality of genes. Neither Friend nor Roninson teaches distinguishing among different variants of an exon. Neither Friend nor Roninson teaches a method for analyzing exon expression in a cell sample, comprising measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of

a plurality, wherein at least one gene in said plurality of different genes comprises an exon possibly having a plurality of different variants, each of said plurality of different variants being a form of said exon generated using a different splice junction of said exon, and wherein the measured expression levels of said different individual exons or different individual multiexons in said gene are sufficient for determining which of said plurality of different variants of said exon is, and which is not, expressed in said cell sample, and determining which of said plurality of different variants of said exon is, and which is not, expressed. Therefore, Applicants respectfully submit that the rejection of claims 13, 160, 218 and 242 under 37 C.F.R. § 102(b) based on Friend and Roninson is erroneous, and should be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 103(a)
SHOULD BE WITHDRAWN

Claims 27, 174, 222 and 246 are rejected under 35 U.S.C. § 103(a) as being obvious over Friend et al., U.S. Patent No. 6,165,709 ("Friend"). Claims 14-21 and 161-168 are rejected under 35 U.S.C. § 103(a) as being obvious over Friend in view of Chee et al., U.S. Patent No. 6,355,431. Applicant respectfully disagrees with the Examiner for the reasons presented below.

A finding of obviousness under 35 U.S.C. § 103(a) requires a determination that the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383, U.S. 1 (1956). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

At the outset, Applicants respectfully submit that claims 222 and 246 have been canceled. The rejection of these claims is therefore obviated.

With respect to the rejection of claims 27 and 174, the Examiner contends that Friend renders these claims obvious in that Friend teaches the limitations of the respective base claims and that it would have been obvious to one of skilled in the art to immobilize different length of polynucleotide probes on an array. As discussed above, Friend does not teach or suggest analyzing the exon expression of a cell sample as claimed. Friend does not teach or

suggest measuring a plurality of different individual exons or different individual multiexons in a gene. Friend does not teach distinguishing among different variants of an exon. Friend does not teach or suggest a method for analyzing exon expression in a cell sample, comprising measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality, wherein at least one gene in said plurality of different genes comprises an exon possibly having a plurality of different variants, each of said plurality of different variants being a form of said exon generated using a different splice junction of said exon, and wherein the measured expression levels of said different individual exons or different individual multiexons in said gene are sufficient for determining which of said plurality of different variants of said exon is, and which is not, expressed in said cell sample, and determining which of said plurality of different variants of said exon is, and which is not, expressed. Thus, Applicants respectfully submit that Friend does not render claims 27 and 174 of the presently claimed invention obvious irrespective of whether it would have been obvious to one of skilled in the art to immobilize different lengths of polynucleotide probes on an array.

With respect to the rejection of claims 14-21 and 161-168, the Examiner contends that Friend renders these claims obvious in that Friend teaches the limitations of the respective base claims and that "it would have been obvious to one having ordinary skill in the art ... to have immobilized different amount of polynucleotide probes on an array" in view of Chee. As discussed above, Friend does not teach or suggest analyzing the exon expression of a cell sample as claimed. Friend does not teach or suggest measuring a plurality of different individual exons or different individual multiexons in each of its genes. Friend does not teach distinguishing among different variants of an exon. Friend does not teach or suggest teaches a method for analyzing exon expression in a cell sample, comprising measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality, wherein at least one gene in said plurality of different genes comprises an exon possibly having a plurality of different variants, each of said plurality of different variants being a form of said exon generated using a different splice junction of said exon, and wherein the measured expression levels of said different individual exons or different individual multiexons in said gene are sufficient for determining which of said plurality of different variants of said exon is, and which is not, expressed in said cell sample, and determining which of said plurality of different variants of said exon is, and which is not,

expressed. Chee teaches compositions and methods for detecting and quantifying a target nucleic acid using a variety of both signal amplification and target amplification techniques. Chee does not provide what is missing in Friend. Thus, Applicants respectfully submit that Friend in view of Chee does not render claims 14-21 and 161-168 of the presently claimed invention obvious.

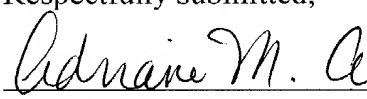
Therefore, Applicants respectfully submit that the rejection of claims 14-21, 27, 161-168, 174, 222, 242 and 246 under 37 C.F.R. § 103 (a) is erroneous, and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that each ground for rejection has been successfully overcome or obviated, and that all pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

Date: April 1, 2003



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Enclosures

EXHIBIT A: MARKED VERSION OF AMENDED CLAIMS
U.S. APPLICATION SERIAL NO. 09/724,538
(ATTORNEY DOCKET NO. 9301-123)

(as amended April 1, 2003)

1. (Amended) A method for analyzing exon expression in a cell sample, comprising measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality of different genes in the genome of an organism from which said cell sample is derived, wherein at least one gene in said plurality of different genes comprises an exon possibly having a plurality of different variants, each of said plurality of different variants being a form of said exon generated using a different splice junction of said exon, and wherein the measured expression [level of each exon or multiexon is not averaged with the measured expression level of one or more different exons or multiexons in the same gene] levels of said different individual exons or different individual multiexons in said gene are sufficient for determining which of said plurality of different variants of said exon is, and which is not, expressed in said cell sample, and determining which of said plurality of different variants of said exon is, and which is not, expressed; thereby analyzing the exon expression of said cell sample.

Claims 2 and 3 have been canceled.

4. (Amended) The method of claim 1, wherein said plurality of different individual exons or different individual multiexons consists of at least 3 different exons or multiexons.

5. (Amended) The method of claim 1, wherein said plurality of different individual exons or different individual multiexons consists of at least 5 different exons or multiexons.

6. (Amended) The method of claim 1, wherein said plurality of different individual exons or different individual multiexons consists of at least two different exons.

11. (Amended) The method of claim 10, wherein said plurality of different individual

exons or different individual multiexons consists of at least 3 different exons.

12. (Amended) The method of claim 10, wherein said plurality of different individual exons or different individual multiexons consists of at least 5 different exons.

30. (Amended) The method of claim 10, wherein [said sequence is] at least one of said plurality of polynucleotide probes comprises a nucleotide sequence complementary to the sequence of a full length exon.

Claim 35 has been canceled.

36. (Amended) The method of claim [35] 1 or 10, wherein said expression levels are measured [as continuous variables and represented] as absolute abundance.

89. (Amended) The method of claim 86, further comprising comparing the expression levels of at least a portion of said plurality of different individual exons or different individual multiexons in said cell sample having been subjected to said perturbation with the expression level of said portion of said plurality of different individual exons or different individual multiexons in a cell sample of the same type not having been subjected to said perturbation.

90. (Amended) The method of claim 89, wherein said comparing comprises determining the difference between the expression level of each exon or multiexon in said portion of said plurality of different individual exons or different individual multiexons in said cell sample having been subjected to said perturbation and the expression level of the corresponding exons or multiexons in said cell sample of the same type not having been subjected to said perturbation.

158. (Amended) The method of claim 157, wherein said plurality of different individual exons or different individual multiexons consists of at least 3 different exons.

159. (Amended) The method of claim 157, wherein said plurality of different

individual exons or different individual multiexons consists of at least 5 different exons.

177. (Amended) The method of claim 157, wherein [said sequence is] at least one of said plurality of polynucleotide probes comprises a nucleotide sequence complementary to the sequence of a full length exon.

Claim 182 has been canceled.

183. (Amended) The method of claim [182] 157, wherein said expression levels are measured [as continuous variables and represented] as absolute abundance.

Claims 214-262 have been canceled.

263. (Amended) The method of [any one of claims 214-217, 226-229, 238-241 and 250-253] claim 10 or 157, wherein said array of polynucleotide probes [further] comprises one or more sets of successive overlapping probes tiled along the longest variant of [an] said exon having a plurality of different variants.

264. (Amended) The method of [any one of claims 216, 228, 240 and 252] claim 10 or 157, wherein said array of polynucleotide probes [further] comprises variant junction probes, wherein each of said variant junction probes is specifically hybridizable to a sequence spanning the splice junction between a different variant of [an] said exon having a plurality of different variants and a neighboring exon.

Claims 268-279 have been canceled.

New claims 280-292 have been added.

EXHIBIT B: CLEAN VERSION OF PENDING CLAIMS
U.S. APPLICATION SERIAL NO. 09/724,538
(ATTORNEY DOCKET NO. 9301-123)

(as amended April 1, 2003)

1. (Amended) A method for analyzing exon expression in a cell sample, comprising measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality of different genes in the genome of an organism from which said cell sample is derived, wherein at least one gene in said plurality of different genes comprises an exon possibly having a plurality of different variants, each of said plurality of different variants being a form of said exon generated using a different splice junction of said exon, and wherein the measured expression levels of said different individual exons or different individual multiexons in said gene are sufficient for determining which of said plurality of different variants of said exon is, and which is not, expressed in said cell sample, and determining which of said plurality of different variants of said exon is, and which is not, expressed; thereby analyzing the exon expression of said cell sample.

4. (Amended) The method of claim 1, wherein said plurality of different individual exons or different individual multiexons consists of at least 3 different exons or multiexons.

5. (Amended) The method of claim 1, wherein said plurality of different individual exons or different individual multiexons consists of at least 5 different exons or multiexons.

6. (Amended) The method of claim 1, wherein said plurality of different individual exons or different individual multiexons consists of at least two different exons.

7. The method of claim 1, 4, 5 or 6, wherein said plurality of different genes consists of at least 100 different genes.

8. The method of claim 1, 4, 5 or 6, wherein said plurality of different genes consists of at least 1,000 different genes.

9. The method of claim 1, 4, 5 or 6, wherein said plurality of different genes consists of at least 10,000 different genes.

10. (Amended) The method of claim 1, wherein said measuring is performed by a method comprising

(a) contacting a positionally-addressable array of polynucleotide probes with a sample comprising RNAs or nucleic acids derived therefrom from said cell sample under conditions conducive to hybridization between said probes and said RNAs or nucleic acids, wherein said array comprises a plurality of polynucleotide probes of different nucleotide sequences bound to different regions of a support, each of said different nucleotide sequences comprising a sequence complementary and hybridizable to a sequence in a different exon or multiexon of said cell sample; and

(b) measuring levels of hybridization between said probes and said RNAs or nucleic acids.

11. (Amended) The method of claim 10, wherein said plurality of different individual exons or different individual multiexons consists of at least 3 different exons.

12. (Amended) The method of claim 10, wherein said plurality of different individual exons or different individual multiexons consists of at least 5 different exons.

13. The method of claim 10, 11 or 12, wherein said plurality of different genes consists of at least 1,000 different genes.

14. The method of claim 10, wherein said plurality of polynucleotide probes consists of at least 100 different polynucleotide probes.

15. The method of claim 10, wherein said plurality of polynucleotide probes consists of at least 1,000 different polynucleotide probes.

16. The method of claim 10, wherein said plurality of polynucleotide probes consists of at least 10,000 different polynucleotide probes.

17. The method of claim 10, wherein said plurality of polynucleotide probes is in the range of 1,000 to 50,000 different polynucleotide probes.

18. The method of claim 10, wherein said positionally-addressable array has in the range of 100 to 1,000 different polynucleotide probes per 1 cm^2.

19. The method of claim 10, wherein said positionally-addressable array has in the range of 1,000 to 10,000 different polynucleotide probes per 1 cm^2.

20. The method of claim 10, wherein said positionally-addressable array has in the range of 10,000 to 50,000 different polynucleotide probes per 1 cm^2.

21. The method of claim 10, wherein said positionally-addressable array has more than 50,000 different polynucleotide probes per 1 cm^2.

22. The method of claim 10, wherein each of said different nucleotide sequences consists of 10 to 1,000 nucleotides.

23. The method of claim 10, wherein each of said different nucleotide sequences consists of 15 to 600 nucleotides.

24. The method of claim 10, wherein each of said different nucleotide sequences consists of 15 to 200 nucleotides.

25. The method of claim 10, wherein each of said different nucleotide sequences consists of 20 to 100 nucleotides.

26. The method of claim 10, wherein each of said different nucleotide sequences consists of 40 to 80 nucleotides.

27. The method of claim 10, wherein each of said different nucleotide sequences consists of 60 nucleotides.

28. The method of claim 10, wherein at least one probe in said plurality of probes contains, in addition to said sequence complementary and hybridizable to a different exon or multiexon, linker sequences.

29. The method of claim 28, wherein said linker sequence comprises a linker sequence between said sequence complementary and hybridizable to a different exon or multiexon and said support.

30. (Amended) The method of claim 10, wherein at least one of said plurality of polynucleotide probes comprises a nucleotide sequence complementary to the sequence of a

full length exon.

31. The method of claim 10, wherein at least one of said plurality of polynucleotide probes comprises a nucleotide sequence complementary and hybridizable to a multiexon.

32. The method of claim 31, wherein the nucleotide sequence of said at least one polynucleotide probe is complementary to a sequence spanning the splice junction between different exons in said multiexon.

33. The method of claim 31, wherein said sequence is complementary to a sequence comprising a full length exon flanked by sequences from adjacent exon or exons in said multiexon.

34. The method of claim 10, wherein said array of polynucleotide probes further comprises control polynucleotide probes comprising sequences complementary and hybridizable to different introns of said plurality of genes in the genome of said organism.

36. (Amended) The method of claim 1 or 10, wherein said expression levels are measured as absolute abundance.

45. (Amended) The method of claim 1 or 10, wherein said organism is a human.

46. (Amended) The method of claim 1 or 10, wherein said organism is a plant.

86. (Amended) The method of claim 1 or 10, wherein said cell sample has been subjected to a perturbation.

87. The method of claim 86, wherein said organism is a human.

88. The method of claim 86, wherein said organism is a plant.

89. (Amended) The method of claim 86, further comprising comparing the expression levels of at least a portion of said plurality of different individual exons or different individual multiexons in said cell sample having been subjected to said perturbation with the expression level of said portion of said plurality of different individual exons or different individual multiexons in a cell sample of the same type not having been subjected to said perturbation.

90. (Amended) The method of claim 89, wherein said comparing comprises determining the difference between the expression level of each exon or multiexon in said portion of said plurality of different individual exons or different individual multiexons in said cell sample having been subjected to said perturbation and the expression level of the corresponding exons or multiexons in said cell sample of the same type not having been subjected to said perturbation.

157. (Amended) The method of claim 1, wherein said measuring is performed by a method comprising

(a) contacting a positionally-addressable array of polynucleotide probes with a sample comprising RNAs or nucleic acids derived therefrom from said cell sample under conditions conducive to hybridization between said probes and said RNAs or nucleic acids, wherein said array comprises a plurality of polynucleotide probes of different nucleotide sequences bound to different regions of a support, each of said different nucleotide sequences comprising a sequence complementary and hybridizable to a sequence in a different exon or multiexon in the genome of an organism from which said cell sample is derived; and

(b) measuring levels of hybridization between said probes and said RNAs or nucleic acids.

158. (Amended) The method of claim 157, wherein said plurality of different individual exons or different individual multiexons consists of at least 3 different exons.

159. (Amended) The method of claim 157, wherein said plurality of different individual exons or different individual multiexons consists of at least 5 different exons.

160. The method of claim 157, 158 or 159, wherein said plurality of different genes consists of at least 1,000 different genes.

161. The method of claim 157, wherein said plurality of polynucleotide probes consists of at least 100 different polynucleotide probes.

162. The method of claim 157, wherein said plurality of polynucleotide probes consists of at least 1,000 different polynucleotide probes.

163. The method of claim 157, wherein said plurality of polynucleotide probes consists of at least 10,000 different polynucleotide probes.

164. The method of claim 157, wherein said plurality of polynucleotide probes is in the range of 1,000 to 50,000 different polynucleotide probes.

165. The method of claim 157, wherein said positionally-addressable array has in the range of 100 to 1,000 different polynucleotide probes per 1 cm^2.

166. The method of claim 157, wherein said positionally-addressable array has in the range of 1,000 to 10,000 different polynucleotide probes per 1 cm^2.

167. The method of claim 157, wherein said positionally-addressable array has in the range of 10,000 to 50,000 different polynucleotide probes per 1 cm^2.

168. The method of claim 157, wherein said positionally-addressable array has more than 50,000 different polynucleotide probes per 1 cm^2.

169. The method of claim 157, wherein each of said different nucleotide sequences consists of 10 to 1,000 nucleotides.

170. The method of claim 157, wherein each of said different nucleotide sequences consists of 15 to 600 nucleotides.

171. The method of claim 157, wherein each of said different nucleotide sequences consists of 15 to 200 nucleotides.

172. The method of claim 157, wherein each of said different nucleotide sequences consists of 20 to 100 nucleotides.

173. The method of claim 157, wherein each of said different nucleotide sequences consists of 40 to 80 nucleotides.

174. The method of claim 157, wherein each of said different nucleotide sequences consists of 60 nucleotides.

175. The method of claim 157, wherein at least one probe in said plurality of probes contains, in addition to said sequence complementary and hybridizable to a different exon or

multiexon, linker sequences.

176. The method of claim 175, wherein said linker sequence comprises a spacer sequence between said sequence complementary and hybridizable to a different exon or multiexon and said support.

177. (Amended) The method of claim 157, wherein at least one of said plurality of polynucleotide probes comprises a nucleotide sequence complementary to the sequence of a full length exon.

178. The method of claim 157, wherein at least one of said plurality of polynucleotide probes comprises a nucleotide sequence complementary and hybridizable to a multiexon.

179. The method of claim 178, wherein the nucleotide sequence of said at least one polynucleotide probe is complementary to a sequence spanning the splice junction between different exons in said multiexon.

180. The method of claim 178, wherein said sequence is complementary to a sequence comprising a full length exon flanked by sequences from adjacent exon or exons in said multiexon.

181. The method of claim 157, wherein said array of polynucleotide probes further comprises control polynucleotide probes comprising sequences complementary and hybridizable to different introns of said plurality of genes in the genome of said organism.

183. (Amended) The method of claim 157, wherein said expression levels are measured as absolute abundance.

212. (Amended) The method of claim 1 or 10, wherein said organism is a fungus.

213. The method of claim 86, wherein said organism is a fungus.

263. (Amended) The method of claim 10 or 157, wherein said array of polynucleotide probes comprises one or more sets of successive overlapping probes tiled along the longest variant of said exon having a plurality of different variants.

264. (Amended) The method of claim 10 or 157, wherein said array of

polynucleotide probes comprises variant junction probes, wherein each of said variant junction probes is specifically hybridizable to a sequence spanning the splice junction between a different variant of said exon having a plurality of different variants and a neighboring exon.

265. The method of claim 86, wherein said perturbation is exposure to a drug.

266. The method of claim 86, wherein said perturbation is a genetic mutation.

267. The method of claim 86, wherein said perturbation comprises mutation of one or more genes and exposure to a drug.

280. (New) The method of claim 32 or 179, wherein each of said different nucleotide sequences consists of 15 to 200 nucleotides.

281. (New) The method of claim 280, wherein each of said different nucleotide sequences consists of 20 to 100 nucleotides.

282. (New) The method of claim 281, wherein each of said different nucleotide sequences consists of 40 to 80 nucleotides.

283. (New) The method of claim 282, wherein each of said different nucleotide sequences consists of 60 nucleotides.

284. (New) A method for analyzing exon expression in a cell sample of an organism, comprising

(a) contacting a positionally-addressable array of polynucleotide probes with a sample comprising RNAs or nucleic acids derived therefrom from said cell sample under conditions conducive to hybridization between said probes and said RNAs or nucleic acids, wherein said array comprises (i) one or more exon specific probes of different nucleotide sequences for each of a plurality of different genes in the genome of said organism, each of said different nucleotide sequences being complementary and hybridizable to a sequence within a different individual exon; and (ii) a variant junction probe for each of a plurality of different possible variants of at least one exon, each of said variants being a form of said exon generated using a different splice junction

of said exon, and each of said variant junction probes being a probe specific to a junction region of said variant and a neighboring exon in a multiexon comprising said variant of said exon, each of said exon specific probes and variant junction probes being bound to a different region of a support; and

(b) measuring levels of hybridization between said probes and said RNAs or nucleic acids.

285. (New) A method for analyzing exon expression in a cell sample of an organism, comprising

(a) contacting a positionally-addressable array of polynucleotide probes with a sample comprising RNAs or nucleic acids derived therefrom from said cell sample under conditions conducive to hybridization between said probes and said RNAs or nucleic acids, wherein said array comprises a plurality of junction specific probes of different nucleotide sequences for each of a plurality of different genes in the genome of said organism bound to different regions of a support, each of said different nucleotide sequences being complementary and hybridizable to a sequence spanning a junction region of a multiexon, and wherein said plurality of junction specific probes comprises a variant junction probe for each of a plurality of different possible variants of at least one exon, each of said variants being a form of said exon generated using a different splice junction of said exon, and each of said variant junction probes being a probe specific to a junction region of said variant and a neighboring exon in a multiexon comprising said variant of said exon; and

(b) measuring levels of hybridization between said probes and said RNAs or nucleic acids.

286. (New) The method of claim 284 or 285, wherein said plurality of different genes consists of at least 100 different genes.

287. (New) The method of claim 286, wherein said plurality of different genes consists of at least 1,000 different genes.

288. (New) The method of claim 287, wherein said plurality of different genes consists of at least 10,000 different genes.

289. (New) The method of claim 284 or 285, wherein each of said different nucleotide sequences consists of 15 to 200 nucleotides.

290. (New) The method of claim 289, wherein each of said different nucleotide sequences consists of 20 to 100 nucleotides.

291. (New) The method of claim 290, wherein each of said different nucleotide sequences consists of 40 to 80 nucleotides.

292. (New) The method of claim 291, wherein each of said different nucleotide sequences consists of 60 nucleotides.